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76595 7590 04/08/2009

LOWRIE, LANDO & ANASTASI, LLP
W2023
ONE MAIN STREET
SUITE 1100
CAMBRIDGE, MA 02142

EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 04/08/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,722	05/17/2001	William Stuart Somers	W2025-700110 / AM100225	2770

TITLE OF INVENTION: CRYSTAL STRUCTURES OF P- SELECTIN, P- AND E-SELECTIN COMPLEXES, AND USES THEREOF

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	07/08/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

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Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

76595 7590 04/08/2009

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,722	05/17/2001	William Stuart Somers	W2025-700110 / AM100335	2770

TITLE OF INVENTION: CRYSTAL STRUCTURES OF P- SELECTIN, P- AND E-SELECTIN COMPLEXES, AND USES THEREOF

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	07/08/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
NOAKES, SUZANNE MARIE	1656	703-011000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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09/859,722	05/17/2001	William Stuart Somers	W2025-700110 / AM100225	2770

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NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 04/08/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 1000 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 1000 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	09/859,722	SOMERS ET AL.	
	Examiner	Art Unit	
	SUZANNE M. NOAKES	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amended claims filed 02/20/09 and the agreed upon examiner's amendment*.

2. ☒ The allowed claim(s) is/are *15,16,36,38-41,43,44,47,48,53-65,73-76 and 78-80*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Diana Collazo on 30 March 2009.

The application has been amended as follows:

In the claims:

1.-14. (Canceled)

15. (Currently Amended) A method for identifying a candidate agent that interacts with P-selectin LE, comprising the steps of:

(a) utilizing the x-ray structural coordinates of P-selectin LE according to Figure 2, Figure 3, or Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, to generate a three-dimensional model;

(b) identifying the amino acid residues forming the active site of said P-selectin LE from the three-dimensional model in step (a) in order to generate a three-dimensional representation of the active site of P-selectin LE,

wherein the x-ray structural coordinates of the active site of said P-selectin LE are selected from the group consisting of:

(i) the x-ray structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than ~~1.5Å~~ 0.5Å;

(ii) the x-ray structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106,

GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

(iii) the x-ray structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;-

(c) employing said three-dimensional representation from step (b) to identify said candidate agent that interacts with the active site of P-selectin LE;

(d) synthesizing said candidate agent;

(e) contacting said candidate agent with said P-selectin LE to determine the ability of said candidate agent to interact or bind with said P-selectin LE;

whereby the detection of the ability of said candidate agent to interact or bind said P-selectin LE, thereby identifies said candidate agent as a agent that interacts with P-selectin LE.

16. (Presently Amended) The method of Claim 15, further comprising the step of:

contacting the candidate agent with P-selectin LE in order to determine the effect the agent has on P-selectin LE activity.

17.-35. (Canceled)

36. (Presently Amended) The method of claim 53, wherein the step of determining the fit between the three-dimensional representation of the active site of P-selectin LE and the three-dimensional structure of the candidate agent comprises performing computer fitting analysis of the candidate agent with the three dimensional representation.

37. (Canceled)

38. (Presently Amended) The method of claim 15, wherein the candidate agent is selected or designed to interact with the active site of P-selectin LE.

39. (Presently Amended) The method of claim 15, wherein the x-ray structural coordinates of the active site of P-selectin LE comprise the structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

40. (Presently Amended) The method of claim 15, wherein the x-ray structural coordinates of the active site of P-selectin LE comprise the structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYSl13, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

41. (Presently Amended) The method of claim 15, wherein the structural coordinates comprise the x-ray structural coordinates of the active site of P-selectin LE crystal according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than ~~1.5Å~~. 0.5Å.

42. (Canceled)

43. (Currently Amended) The method of claim 15, wherein the ± a root mean square deviation from the backbone atoms of parts ii) or iii) for said amino acids is not more than 1.0Å .

44. (Currently Amended) The method of claim 15, wherein the ± a root mean square deviation from the backbone atoms of parts ii) or iii) for said amino acids is not more than 0.5Å.

45. (Canceled)

46. (Canceled)

47. (Previously Presented) The method of claim 40, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å.

48. (Previously Presented) The method of claim 40, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

49.-52. (Canceled)

53. (Presently Presented) The method of claim 15, wherein the identifying step (c) comprises determining a fit between the three-dimensional representation of the active site of P-selectin LE and a three-dimensional structure of the candidate agent.

54. (Previously Presented) The method of claim 15, wherein the three dimensional model is generated using the relative structural coordinates according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

55. (Previously Presented) The method of claim 15, wherein the three dimensional model is generated using the relative structural coordinates according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

56. (Previously Presented) A method for identifying a candidate agent that interacts with P-selectin LE, comprising the steps of:

(a) providing a three-dimensional structure of P-selectin LE, the three-dimensional structure being obtained by subjecting a crystal comprising P-selectin LE to x-ray diffraction and collecting data sufficient to determine the three-dimensional structure of said P-selectin LE, wherein said P-selectin LE consists of the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9, and said crystal is characterized by space group $P2_1$ with unit cell parameters of a=81.0Å, b=60.8Å, c=91.4Å, and beta=103.6°; or by space group $P2_1$ with unit cell parameters of a=81.1Å, b=60.5Å, c=91.4Å, and beta=103.3°; or by space group I222 with unit cell parameters of a=63.4Å, b=96.8Å, and c=187.3Å;

(b) generating a three dimensional model from said three-dimensional structure of P-selectin LE;

(c) identifying the amino acid residues forming the active site of P-selectin LE from the three-dimensional model in step (b) in order to generate a three-dimensional representation of the active site of P-selectin LE;

(d) employing said three-dimensional representation from step (c) to design or select the candidate agent that interacts with P-selectin LE; and

(e) contacting said candidate agent with said P-selectin LE to determine the ability of said candidate agent to interact or bind said P-selectin LE;

whereby the detection of the ability of said candidate agent to interact or bind said P-selectin LE thereby identifies said candidate agent as an agent that interacts with P-selectin LE.

57. (Previously Presented) The method of claim 56, further comprising contacting the candidate agent with P-selectin LE in order to determine the effect the agent has on P-selectin LE activity.

58. (Previously Presented) The method of claim 56, wherein the three dimensional structure of P-selectin LE comprises the x-ray structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å .

59. (Previously Presented) The method of claim 56, wherein the three dimensional structure of P-selectin LE comprises the x-ray structural coordinates according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å .

60. (Previously Presented) The method of claim 56, wherein the three dimensional structure of P-selectin LE comprises the x-ray structural coordinates according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

61. (Previously Presented) The method of claim 56, wherein the x-ray structural coordinates of the amino acid residues forming the active site of P-selectin LE according to step (c) are selected from the group consisting of:

(i) the x-ray structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

(ii) the x-ray structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

62. (Previously Presented) The method of claim 56, wherein the P-selectin LE in the crystal is complexed with SLe^x.

63. (Previously Presented) The method of claim 62, wherein the P-selectin LE consists of the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ 1D NO:9, and the crystal has space group $P2_1$ with unit cell parameters of a=81.1Å, b=60.5Å, c=91.4Å, and beta=103.3°.

64. (Previously Presented) The method of claim 56, wherein the P-selectin LE in the crystal is complexed with a PSGL-1 peptide.

65. (Previously Presented) The method of claim 64, wherein the P-selectin LE comprises the amino acid sequence of SEQ 1D NO:6, SEQ ID NO:8 or SEQ ID NO:9, and the crystal has space group I222 with unit cell parameters of a=63.4Å, b=96.8Å, and c=187.3Å.

66.-72. (Canceled)

73. (Currently Amended) The method of ~~claim 56~~ any of claims 58-60, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å .

74. (Currently Amended) The method of ~~claim 56~~ any of claims 58-60, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

75. (Previously Presented) The method of claim 56, further comprising detecting the ability of the candidate agent to bind *in vitro* or *in vivo* to the active site of P-selectin LE.

76. (Previously Presented) The method of claim 56, further comprising synthesizing said candidate agent.

77. (Canceled)

78. (Previously Presented) The method of claim 15, further comprising detecting the ability of the candidate agent to bind in vitro or in vivo to the active site of P-selectin LE.

79. (Previously Presented) The method of claim 39, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å .

80. (Previously Presented) The method of claim 39, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

Withdrawal of Previous Rejections/Objections

2. The rejection of claims 15, 16, 36-41, 43-50 and 53-65 under 35 U.S.C. 112 1st paragraph, scope of enablement and written description (see previous Office action, Sections 5 and 6) is withdrawn in view of the amendments to the claims filed 02/25/2009 and the instant amendments recited above. The instant claims 15, 16, 36-41, 43-50 and 53-55 are now limited to *in silico* screening methods rather than utilizing P-selectin LE crystals. Said methods utilize Figures 2 (±0.5Å rmsd), Figures 3 or 5 (±0.5-1.5Å rmsd) and specific amino acids for modeling candidate compounds into the active site. Thus, the claims as amended overcome the both rejections of record. Claims 56-65 remain drawn to utilizing specific P-selectin LE crystals, however, the crystals are identified by specific sequences, space groups and unit cell parameters and thus also overcome the written description and scope of enablement rejections of record.

3. The rejection of claims 66-69 and 70-72 under 35 U.S.C. 103(a) (see previous Office action, Section 8) is moot in view of the cancellation of said claims.

4. All previous claim objections are withdrawn in view of the amendments to the claims on 02/25/2009.

5. The rejection of claims 66-72 under 35 U.S.C. 112 1st paragraph, written description, (see previous Office action, Section 10) is moot in view of the cancellation of said claims.

Reasons for Allowance

6. The following is an examiner's statement of reasons for allowance: The instant claims are drawn to *in silico* methods of utilizing P-selectin LE in apo form (Figure 2), and complexed to Sle^X (Figure 3) or PSGL-1 (Figure 5) for to screen candidate compounds, or utilizing specific crystals or co-crystals as described in claims 56-65 to generate three-dimensional structures which are utilized to screen *in silico* candidate compounds which bind said P-selectin LE. The later claims (56-65) are novel and non-obvious in and of themselves because P-selectin LE has never been crystallized previously, and specifically not with these particular sequences, space groups and unit cell parameters. The closest prior art available is Graves et al.(cited on PTO-892, 07/03/2006) who crystallized E-selectin LE, however, because of the extreme unpredictability in science of protein crystallography, the crystallization of one protein does not necessarily aid in the crystallization of another. With regard to the *in silico* claims, said claims are also non-obvious and novel because while E-selectin LE is closely related, the specific three-dimensional structure of the binding pocket is clearly lined with different amino acids than those disclosed by Graves et al. than those listed in the claims. In addition, the identified amino acids of the binding pocket are not obvious from prior art. **Thus, the allowed claims are 15,16, 36, 38-41, 43, 44, 47, 48, 53-65, 73-76 and 78-80.**

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably

accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
31 March 2009